Frequency and Importance of Hypoglycemia in the Neonate

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Neonatal hypoglycemia is underestimated even today, with regard to its frequency and to its damaging effect upon brain development, which may well be preventable. One of the factors responsible for this neglect may be the erroneous belief that neonatal hypoglycemia has to show specific symptoms. However contrary to hyperbilirubinemia which is obvious, neonatal hypoglycemia occurs mostly without any specific signs or may even be asymptomatic. It is not diagnosed clinically and requires laboratory verification. Often the damage by hypoglycemia is increased by other risk factors, especially by hypoxemia. The definition of hypoglycemia is based on CORNBLATH et al. (3).

The impairing effect of hypoglycemia is dependent of its severeness and duration. We still do not know the time, i.e. how long a hypoglycemic state can be tolerated without lasting consequences.

Neonatal hypoglycemia usually occurs in the first days after birth, especially if energy intake is insufficient. The danger of hypoglycemia may exist even during the first hour of life.

A recently published study of PRIBYLOVA (6) corroborates this, especially in SGA infants. The initial blood glucose of the SGA infants after birth is 20 % lower than that of the controls, 74mg/100ml versus 93mg/100ml. During the first hour of life there is a steep decrease in blood glucose amounting 58 % in the SGA infants versus 41 % in the controls. Also our investigations in regard to early decrease of blood glucose are consonant with her findings (6).

The incidence of neonatal hypoglycemia according to our results in Bonn is represented in Tab. 1 . In 26 % on average of all neonates (n = 250) admitted to our hospital during the last year hypoglycemia was proven to be present at least on one occasion. In more than 50 % of the cases a hypoglycemia was already proven at the first examination after admission to our hospital or in an obstetric department after birth. In one third of the infants hypoglycemia relapsed at least once, and that even with treatment.

SGA infants are at greatest risk for hypoglycemia, nearly 50 % of them are in danger. These actual results confirm those in the literature (2, 8).

Tab. 1. Incidence of neonatal hypoglycemia
Admissions of one year to the University Children's Hospital Bonn

A. Full term infants		
Appropriate-for-gestational-age	23 %	(22/95)
Small-for-gestational-age	38 %	(6/16)
Large-for-gestational-age	38 %	(5/13)
B. Preterm infants		
Appropriate-for-gestational-age	20 %	(20/101)
Small-for-gestational-age	44 %	(11/ 25)

0300-5577/82/0102-0013 $ 2.00

Most of the hypoglycemic infants were asymptomatic or had non-specific symptoms, as episodes of cyanosis, apnea, irritability or apathy. So the diagnosis was made only after the laboratory determination for glucose. Without immediate appropriate treatment these infants would have been in great danger of persisting and even worsening hypoglycemia. Therefore it seems justified to recommend immediate blood glucose estimations in all neonates admitted to a pediatric clinic and to repeat this screening in regular intervals.

As long as in most cases of mental subnormality the causes remain obscure, every chance should be taken to eliminate possible pathogenetic factors. The damaging effect of persistent hypoglycemia for the developing brain - especially in the presence of other risk factors as hypoxia - cannot be questioned (2).

The following newborn infants are at special risk of hypoglycemia: (1) Small-for-gestational-age, males are more at risk than females; (2) preterm or low-birth-weight; (3) twins, especially the smaller of them; (4) neonatal stress and hypoxia; (5) preceding unexplained neonatal death; (6) diabetic mothers, and (7) beta-sympathomimetic tocolytic therapy of the mother.

No substance normally present in the blood can replace glucose as a substrate for the brain's energy metabolism and the normal functioning of the central nervous system.

The significantly higher rate of hypoglycemia in SGA preterms than in all other neonates points to the lack of energy reserves as one of the main causal factors. The liver is struck most severely by intrauterine nutritional deprivation (2, 5). The ratio brain weight/liver weight normally 3:1 may be increased up to 6:1. Here has to be considered that the brain is growing at its fastest rate in the perinatal period (2, 4).

Among the possible pathogenetic mechanisms of neonatal hypoglycemia in SGA infants are the following: (1) Insufficient glycogen reserves of the liver; (2) hypermetabolism; (3) brain ultilization of glucose exceeding glucose-producing capacity of the undersized liver; (4) abnormally rapid disappearance of glucose from the blood, and (5) reduced or lack of fat reserves.

For assessment of nutritional status of the neonates and therefore as indicator of hypoglycemic risk the ponderal index of ROHRER (7) or the weight-length ratio can be used:

$$\text{Ponderal index} = \frac{100 \times \text{weight in g}}{(\text{supine length in cm})^3}$$

In SGA infants, the ROHRER index demonstrates clearly the undernourished state (1).

In summarizing are drawn the following conclusions: The knowledge of the dynamics of blood glucose with its rapid decrease after birth contributes to the understanding of neonatal hypoglycemia. A subsequent hypoglycemia can be foreseen already shortly after birth

from the blood glucose estimations. In SGA infants who have few reserves of energy a state of hypoglycemia will persist and worsen unless treated. Furthermore there is always a risk of relapse,which can occur even under treatment. Therefore regular screening of blood glucose is recommend in: (1) all SGA infants, (2) AGA risk infants, and (3) all neonates admitted to a children's hospital. Hypoglycemia cannot be diagnosed clinically; it may be asymptomatic or occur with nonspecific symptoms. Therefore it requires laboratory analysis and a response to glucose therapy.

While many are already screening for rare diseases which have difficult or in contrast to hypoglycemia,no therapy,few screen for hypoglycemia which is relatively common and easy to treat successfully.

Since one of my main interests is in child development and preventive pediatrics,I am especially concerned with the prevention of neurological and mental handicaps. Since in many cases of mental subnormality so little is known about the causes (1),one should at least try to eliminate all possible risk factors that could contribute to it. I consider persistent or recurring neonatal hypoglycemia a dangerous impairing factor for the rapidly growing brain.

The significant higher incidence of hypoglycemia in SGA infants should alert the neonatologist and the obstetrician to start feeding immediately after birth.Because of the risk of relapse treatment may not be discontinued f.e. during tranportation of the baby.

We still do not know how long a hypoglycemic state can be tolerated without lasting consequences; therefore prevention should be the main goal. However neonatal hypoglycemia if diagnosed early and treated appropriately might well lead to a better outcome than previously reported (3).

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